Hg (0.1%), as compared to baseline measurements. After topical application of 8-iso PGE_2 the IOP was lower ($p<0.01$) in the treated eyes of 6 N monkeys for 4 hrs, with a maximum difference of 3.2±0.2 mmHg, as compared to the fellow contralateral control eyes. The pupil size was smaller ($p<0.01$) for 4 hrs, up to 1.0±0.2 mm. Compared with vehicle-treated contralateral control eyes, C was greater ($p<0.005$) by 48% at 2 hr after a single dose of 0.1% 8-iso PGE_2. F was unchanged ($p<0.10$) over a period of 4 hrs after drug administration. Mild eyelid edema, conjunctival edema, hyperemia, and discharge appeared in some eyes treated with the 0.1% concentration.

Table 1A shows that 8-iso PGE_2 administered to the normal monkey eye lowers IOP significantly by 20.3% and increases outflow facility by 43.1%, an amount sufficient to account for the fall of IOP. By contrast, in Table 1B latanoprost in the normal monkey eye also lowers IOP significantly (by 10.8%), but the drug has no significant effect on outflow facility. The lack of a major effect on outflow facility of latanoprost in the primate eye is in agreement with studies in the literature by other investigators.

TABLE 1

A. Effect of 0.1% 8-isoPGE_2 on Outflow Facility in 6 Normal Monkeys (2 hours after treatment)

	Intraocular Pressure Mean ± SEM mmHg	Outflow Facility Mean ± SEM μl/ml/mmHg
Treated eyes (drug)	13.0 ± 0.7*	0.83 ± 0.10*
Baseline	16.3 ± 1.1	0.58 ± 0.03
Control eyes (vehicle)	15.7 ± 0.5	0.56 ± 0.06
Baseline**	15.7 ± 0.6	0.51 ± 0.04

B. Effect of 0.005% latanoprost on Outflow Facility in 6 Normal Monkeys (1 hour after treatment)

	Intraocular Pressure Mean ± SEM mmHg	Outflow Facility Mean ± SEM μl/min/mmHg
Treated eyes (drug)	13.2 ± 0.7*	0.76 ± 0.08
Baseline	14.8 ± 0.7	0.62 ± 0.07
Control eyes (vehicle)	15.0 ± 0.8	0.60 ± 0.07
Baseline**	15.7 ± 0.3	0.73 ± 0.08

*Significantly different as compared with either baseline values or vehicle-treated eyes (two-tailed paired t-test, p. < 0.05.
**Baseline measurements made in the same monkeys at the same time one day prior to drug treatments

Table 2 shows the effect of 8-iso PGE_2 on IOP and outflow facility in glaucomatous monkey eyes. Because of the individual variability in laser-induced glaucomatous monkey eyes, the IOP and facility measurements are expressed in the table as ratios (value of the drug-treated eye÷the value of the vehicle-treated eye). The ratios were calculated from the values of the same glaucomatous monkey eye determined immediately prior to administration of the drug or the vehicle (time 0 hrs.), and the values at 2 hours after administration of the drug or vehicle. The data in Table 2 show that in the primate, administration of 8-iso PGE_2 to glaucomatous eyes significantly lowers IOP (by 13.8%) and significantly increases outflow facility (by 38.8%), which is of sufficient magnitude to account for the fall in IOP. Thus the mechanism of lowering IOP by 8-iso PGE_2 in both normal and glaucomatous eyes is primarily due to an increase in aqueous humor trabecular outflow.

TABLE 2

Effect of 0 1% 8-iso PGE_2 on IOP and Outflow Facility Responses in 8 Glaucomatous Monkey Eyes (Unilateral)

	Intraocular Pressure (drug-treated/ vehicle-treated)		Outflow facility (drug-treated/ vehicle treated)	
Time	0 hr	2 hr	0 hr	2 hr
Response Ratio (± SEM)	0.976 ± 0.002	0.843* ± 0.0498	1.041 ± 0.0498	1.445** ± 0.161
% Change by drug	—	13.8% decrease	—	38.8% decrease

Significantly different as compared to 0 hr, paired t-test, $p < 0.01$*, <0.10**

EXAMPLE II

IOP was measured one hour before and at intervals up to six hours after a single dose of 8-iso PGE, (the 13, 14 dihydro derivative of 8-iso PGE_2), 8-iso PGE_2, or 8-iso $PGF_{2\alpha}$ in laser-induced glaucomatous eyes in cynomolgus monkeys (wherein only one eye is rendered glaucomatous and the other serves as a control). Following one day of baseline IOP measurement, a single 25 μl dose of either (i) 0.1 percent 8-iso PGE_1, or (ii) 0.1 percent 8-iso PGE_2, or (iii) 0.1 percent 8-iso $PGF_{2\alpha}$, was topically applied to the glaucomatous eye in groups of 4 or 8 monkeys. It was found that 8-iso PGE_1 (0.1 percent) reduced IOP ($p<0.05$) for up to four hours in glaucomatous monkey eyes (n=4). The maximum reduction in IOP was 5.3±0.8 (mean±SEM) mm Hg at 2 hours after dosing. 8-iso PGE_2 (0.1 percent) reduced IOP ($p<0.05$) for 5 hours with a maximum reduction in IOP of 6.6±0.8 mm Hg at 2 hours after dosing (n=8). After 0.1 percent 8-iso $PGF_{2\alpha}$, a significant ($p<0.05$) reduction in IOP occurred only at 1 hour with the maximum reduction in IOP of 3.3±0.9 mm Hg (n=4). The results are shown in Table 3. Based on these studies, of the compounds tested, 8-iso PGE_2 appears to have the greatest and 8-iso $PGF_{2\alpha}$. the least activity in decreasing IOP in glaucomatous monkey eyes.

TABLE 3

Intraocular Pressure (treated - baseline) (mean mm Hg ± SEM)

iso PG, 0.1%	n	1 hr	2 hr	4 hr	6 hr
8-iso PGE_1	4	−3.3 ± 1.3	−5.3 ± 0.8*	−2.3 ± 0.5*	−1.3 ± 0.9
8-iso PGE_2	8	−4.5 ± 0.9**	−6.6 ± 0.8**	−2.9 ± 0 6**	−1.2 ± 1.2
8-iso $PGF_{2\alpha}$	4	−3.3 ± 0.8*	−1.8 ± 1.1	−0.8 ± 1.7	0.3 ± 0.5

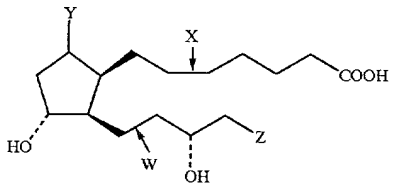
*$p < 0.05$
**$p < 0.005$

Various publications are cited herein, the contents of which are hereby incorporated by reference in their entireties.

We claim:

1. A method for decreasing intraocular pressure comprising administering a therapeutically effective amount of an 8-iso prostanoid having the following Formula I:

Formula I



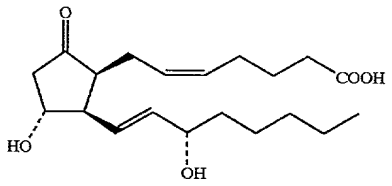
where bond W is selected from the group consisting of a single covalent bond and a double covalent bond, bond X is selected from the group consisting of a single covalent bond and a double covalent bond, substituent Y is selected from the group consisting of a hydroxyl group having either α or β orientation relative to the five-membered ring and a keto function, and substituent Z is a hydrocarbon group selected from the group of aliphatic, aromatic, or a combination of aliphatic and aromatic hydrocarbon, to a patient in need of such treatment.

2. The method of claim 1 wherein the 8-isoprostanoid is administered topically.

3. The method of claim 2 wherein the 8-iso prostanoid is administered as a composition comprising between 0.005 to 1 percent 8-iso prostanoid.

4. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

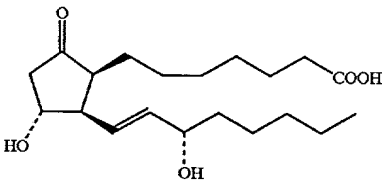
Formula II



or a derivative thereof.

5. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

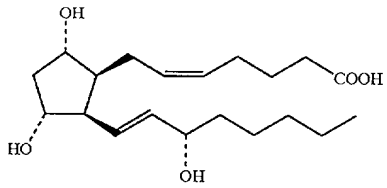
Formula III



or a derivative thereof.

6. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

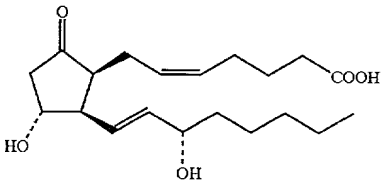
Formula IV



or a derivative thereof.

7. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

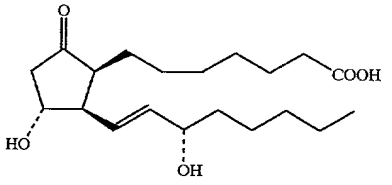
Formula II



or a derivative thereof.

8. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

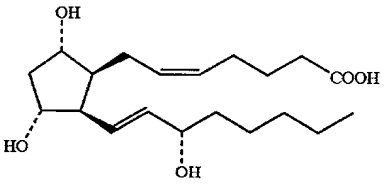
Formula III



or a derivative thereof.

9. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

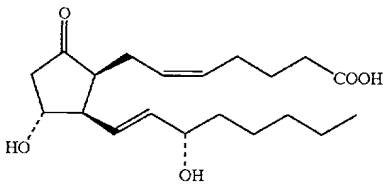
Formula IV



or a derivative thereof.

10. The method of claim 3, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

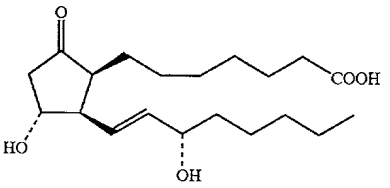
Formula II



or a derivative thereof.

11. The method of claim **3**, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

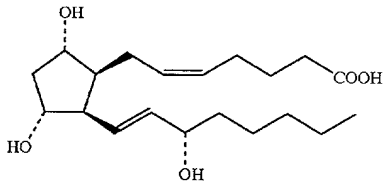
Formula III



or a derivative thereof.

12. The method of claim **3**, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

Formula IV



or a derivative thereof.

13. The method of claim **4**, wherein the derivative is an ester derivative.

14. The method of claim **5**, wherein the derivative is an ester derivative.

15. The method of claim **6**, wherein the derivative is an ester derivative.

16. The method of claim **7**, wherein the derivative is an ester derivative.

17. The method of claim **8**, wherein the derivative is an ester derivative.

18. The method of claim **9**, wherein the derivative is an ester derivative.

19. The method of claim **10**, wherein the derivative is an ester derivative.

20. The method of claim **11**, wherein the derivative is an ester derivative.

21. The method of claim **12**, wherein the derivative is an ester derivative.

* * * * *